and polyvinyl pyrrolidone and/or polyethylene oxide, as suggested by the Examiner. The present claims are also directed to an antiviral drug as nasal drops including a biocompatible antioxidant, as supported by the present application page 3 line 24. Applicant submits that the present application enables a person skilled in the art to make and use the present invention with any biocompatible antioxidant, without undue experimentation. With reference to the factors the Examiner kindly enumerated, many biocompatible antioxidants are (v) known in the art and are well-characterized, as is their toxicity, and so would require little (i) experimentation to use in the present invention. Very little direction or guidance (ii) would be required to include a biocompatible antioxidant in the present invention. Particularly in the pharmaceutical field (iv, vii), biocompatible antioxidants are known and well characterized, as they may be useful in research as well as therapy. Finally, (viii) the present claims are clear as to those components that must be use with the biocompatible antioxidant. Applicant submits that one skilled in the art would be able to determine from the prior art whether an antioxidant is suitable for the purposes of the present invention. Applicant submits that to restrict the invention to a single antioxidant would unfairly limit the invention to less than described, in particular as the disclosure of Trilon B as an antioxidant in the application is clearly meant to be but an example of a biocompatible antioxidant. Accordingly, Applicant requests the rejection be withdrawn.

In paragraph 5 of the Action, the Examiner rejects Claims 6, 7 and 10 to 12 (similar to new claim 14) as obvious under 35 USC 103 over Cymbalista (U.S. Patent No. 4,647,545, March 3, 1987) in view of Evans (U.S. Patent No. 4,710,376, December 1, 1987) and Gray (U.S. Patent No. 4,855,238, August 8, 1989). Specifically, the Examiner states that Cymbalista discloses compositions having beta interferon and 0.5% to 10% (w/v) polyvinyl pyrrolidone as in the present invention, but not recombinant interferon, an

antioxidant or a polymer of polyethylene oxide. However, in combination with Evans' teaching of a topical therapeutic system comprising recombinant interferon, an antioxidant system, and polyethylene glycol (i.e. polyethylene oxide) and Gray's teaching of enhanced stability of beta interferon, it would have been obvious to one skilled in the art to use recombinant interferon, a biocompatible polymer, polyethylene glycol and an antioxidant in the composition taught by Cymbalista.

Applicant respectfully submits the present invention is not obvious and is patentable over Cymbalista in view of Evans and Gray. Cymbalista discloses stabilized b-interferon ("b-IFN"), purified from cultured fibroblasts, in compositions for intravenous administration that may be transported and stored in lyophilized form or after resuspension in a suitable diluent, comprising a buffered solution of highly purified b-IFN, conventional excipients and polyvinyl pyrrolidone. Cymbalista also discloses a method for making the stable IFN composition by dialyzing an IFN solution into acetate buffer, sterile filtering the dialysed b-IFN, dispensing into glass vials, lyophilizing and sealing the vials for storage at 4C. The IFN of Cymbalista is likely resuspended for injection into subjects, in view of the sterile filtration procedures discussed therein. The problem addressed by Cymbalista was that of the instability of IFN solutions prepared from lyophilized IFN, specifically the rapid loss of IFN activity in resuspended preparations. The problem was solved by Cymbalista by lyophilizing the IFN in polyvinyl pyrrolidone, with excipients such as mannitol and HSA (human serum albumin).

In Cymbalista, the stability of the compositions is disclosed as complete within the system described. No suggestion or motivation to add an antioxidant to further stabilize the composition is disclosed; rather, Cymbalista emphasizes maximizing IFN stabilization by specific molecular weights of polyvinyl

pyrrolidone (column 3 line 66 to column 4 line 4, for instance). Furthermore, the addition of further compositions in order to stabilize the use of the resuspended lyophilized IFN is not discussed in Cymbalista. Applicant submits that, rather than motivating one of skill in the art to add additional substances, Cymbalista teaches that stabilization of its specific lyophilized IFN and IFN resuspensions requires no further stability aids. Yet Evans discusses the inclusion of a complex redox system (discussed below) in order to stabilize IFN preparations by inhibiting or forestalling oxidative degradation of the IFN (Evans column 2 lines 60 to 64). In the pharmaceutical field simpler is generally better, particularly for IV preparations, because the more substances involved in an injected pharmaceutical composition the greater the chance for idiosynchratic or other effects that diminish the usefulness of the composition. For support of this statement see for instance the Evans reference discussed by the Examiner, column 3 lines 3 to 7. Certainly, neither Cymbalista nor Evans suggest or teach in any way the application of the present IFN preparations to the nasal mucosa as anti-viral nose drops. Applicant submits therefore that one skilled in the art would not be taught or motivated to combine Cymbalista with Evans and/or Gray in this instance, and that the obviousness rejection is overcome accordingly.

Furthermore, with respect to the Evans reference, the Examiner states that Evans teaches a topical therapeutic composition comprising a recombinant interferon, an oxidation inhibitor system (an antioxidant) and polyethylene glycol, ie polyethylene oxide, citing claims 1-5 of Evans. Applicant notes that Evans claim 5 discloses a composition where a water soluble polymer of the invention is derived from polyethylene glycol. See for instance Evans column 5 line 62 to column 6 line 26, wherein Evans explains that water soluble polymers suitable for Evans' invention are modified to contain reducing and oxidizing moieties, and column 6 line 27 to column 11 line 58, wherein some of the

modifications are described. So in part Evans discloses polyethylene glycol derivatives for use in the redox system of Evans' invention. Polyethylene glycol is also described as an additive to Evans' invention at column 12 line 54 as a compound that may be added to Evans' invention, however, only in conjunction with the polymeric redox system described as essential to the patent. Furthermore, Evans states that to include polyethylene glycol in IFN compositions "requires special handling procedures for incorporating the interferon into the vehicle base." At room temperature and below, the polyethylene glycols preferred for use with Evans' invention are semi-solid pastes rather than liquids, so (Evans column 13 lines 8-9) a polyethylene glycol based ointment can be prepared by combining the interferon with the glycols when both components have been heated to an elevated temperature. Applicant submits that one skilled in the art would, upon reading Evans, not be taught to include polyethylene glycol in a nasal drop formulation of a drug, nor be taught to use simple antioxidants in place of the complex redox system described therein.

Finally, the Gray patent is cited only to state advantages of using b-IFN, and would not motivate or teach one skilled in the art to prepare the nasal drugs of the present invention.

In response to paragraph 6 of the Action, Applicant notes that the typographical error has been corrected in the present claims, so that all claims refer to "polyvinyl pyrrolidone".

In light of the foregoing response, all of the outstanding objections and rejections of record have been overcome. Application respectfully submits that this application should now be in condition for allowance and respectfully requests favorable consideration.

Respectfully submitted,

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Date

Attorney for Applicants
Valerie Neymeyer-Tynkov
c/o Ladas & Parry
224 South Michigan Avenue
Chicago, Illinois 60604
(312) 427-1300
Reg. No. 46,956